

## Exhibit "A"

1. Black's Medical Dictionary Article
2. Lipoma Medical Articles
3. Fibroid Medical Articles

failure to grow in childhood, weight loss, abdominal bloating and discomfort, anemia, and the passage of fatty, foul-smelling stools that float to the top of the toilet water. The disorder often can be diagnosed on the basis of symptoms and confirmed by examining a small sample of intestinal tissue. As the disease progresses, the fingerlike villi that line the intestinal walls, and from which nutrients are absorbed into the bloodstream, will become flattened and smooth. This impairs the body's ability to absorb a variety of nutrients, explaining the weight loss and nutritional deficiencies that are common to celiac disease.

Treatment involves consuming a gluten-free diet. In addition to breads and other obvious sources of wheat or rye flours, gluten is added to a wide variety of foods, including things like soups, gravies, ice cream, and many other commercial products. Thus, food labels should be carefully examined for the addition of gluten or grain products. Patients with celiac disease often can benefit from nutritional counseling, especially since the disorder often results in a variety of nutritional deficiencies, including anemia, which require vitamin and mineral supplements. In some severe cases, steroid drugs may be prescribed for a period to help promote recovery of the intestine.

**Tropical Sprue.** This disorder is uncommon in the United States, although it is seen occasionally among people from the Caribbean, India, and Southeast Asia. The cause is unknown, although it is assumed to be related in some way to nutritional deficiency and environmental factors, including infection, intestinal parasites, or perhaps consumption of certain food toxins.

Tropical sprue causes varied symptoms, including anemia and other nutritional deficiencies, weight loss, and diarrhea. A sore tongue also is common, as are symptoms of other malabsorption syndromes, such as passage of fatty stools. Diagnosis is based on an analysis of intestinal tissue samples, showing deformities in the intestinal villi.

Treatment consists of folic acid and long-term antibiotics. Treatment may be continued for 6 months or longer, depending upon the severity of the disease.

**Whipple's Disease.** This is a relatively rare disorder, mostly affecting middle-aged men. Symptoms include severe malabsorption, nutritional deficiencies, chronic low-grade fever, diarrhea, joint pain, weight loss, and darkening of the skin pigmentation. Many other organs, including the brain, heart, lungs, and eyes, may be affected. The cause of Whipple's disease is unknown, although it is as-

sumed to be from some sort of bacteria. At one time, the disease was invariably fatal; now, however, most cases can be cured or effectively controlled with long-term use of antibiotics, such as tetracycline.

**Miscellaneous Causes.** In addition to specific intestinal abnormalities or deficiencies, a number of other disorders can hinder absorption. Congestive heart failure, scleroderma, intestinal lymphoma, liver disease, and bacterial overgrowth are among the numerous conditions that can hinder absorption from the small intestine. Intestinal damage from radiation therapy or certain drugs also may affect absorption. Whenever there is unexplained weight loss, abdominal discomfort or symptoms, and nutritional deficiencies, malabsorption should be suspected.

## \*Intestinal Obstruction

Intestinal obstruction can result from either a mechanical blockage or from a type of intestinal paralysis (adynamic ileus) in which peristalsis (the coordinated muscular contractions that propel food through the gastrointestinal tract) ceases. Mechanical blockages may be caused by tumors, adhesions or scarring, congenital abnormalities, and strangulated hernia, among other factors. Paralytic ileus, more common in the colon than in the small intestine, may be caused by infection, surgery or other trauma, or certain metabolic disorders that affect muscle function; for example, potassium deficiency (hypokalemia).

The obstruction may be complete or partial; in either instance, symptoms are likely to include vomiting, bloating, and abdominal cramps. If the obstruction is high, the vomiting is likely to be more severe and may result in a biochemical imbalance and shock. If the obstruction is complete, the vomitus may resemble feces. Complete obstruction also results in constipation and severe bloating caused by a buildup of intestinal gas. These symptoms also may be present in a partial obstruction, but not to such a severe degree. Obstruction caused by a strangulated section of intestine, usually the result of a hernia, may lead to gangrene and perforation of the intestine—a life-threatening situation.

Diagnosis is based on symptoms and x-ray studies to locate the site of obstruction. Treatment involves surgical correction of the obstruction as soon as possible, especially if it involves a strangulated hernia or other condition likely to lead to tissue death. The intestinal contents are removed through an intestinal tube. Antibiotics may be given to prevent or treat infection.

lowing or there are other serious symptoms. In these unusual circumstances, surgical removal of the diverticula may be required.

### Esophageal Rupture

Infrequently, the esophagus will become ruptured or torn, resulting in bleeding. Most esophageal ruptures occur in the lowermost portion and may be caused by retching or vomiting. The bleeding frequently will stop on its own; if not, the rupture will have to be sutured or ligated. Perforation or rupture of the upper esophagus is more serious and requires emergency surgery to repair the tear, and drainage of blood from the chest cavity.

### Congenital Defects

Several congenital malformations of the esophagus occur in a small number of infants. One of the most serious is esophageal atresia, in which the esophagus ends in a self-contained pouch rather than the stomach. This condition requires surgery shortly after birth to link the esophagus and stomach and to permit the normal flow of food. Other possible congenital malformations include narrowing or strictures of the esophagus, which make it difficult for the infant to swallow, especially when solid foods are introduced. These often can be corrected by dilation.

## DISORDERS OF THE SMALL INTESTINE

DIGESTION IS COMPLETED in the small intestine and the usable nutrients from food are absorbed into the circulation from this organ. Understandably, then, many of the disorders affecting it involve these processes; including such things as ulcers (discussed in an earlier section), intestinal obstruction, and the various malabsorption syndromes. Intestinal inflammatory disorders, such as ileitis and enteritis, also are relatively common.

### Malabsorption Syndromes

Many different conditions and circumstances affect the ability of the small intestine to absorb nutrients adequately. Examples include a fault in the digestive process, such as a failure to produce enzymes needed to break down certain foods; structural defects or tumors in the intestine itself; inflammatory processes, intestinal infections, and other diseases; and congenital defects. Injury or surgical removal of portions of the small intestine also may result in absorption problems.

Symptoms vary according to the cause, but the most common are weight loss; abdominal discomfort, including cramps, gas, and bloating; diarrhea; abnormal stools; nutritional deficiencies; anemia; and in children, a failure to thrive or grow. Specific malabsorption disorders include the following.

**Lactose Intolerance.** This is a common disorder caused by a lack of lactase, an enzyme secreted in the walls of the small intestine that is needed to break down lactose, the sugar in cow's milk. It is most common among blacks and people of Asian origin, although it is estimated that up to 75 percent of

all adults (excluding those of northern European extraction) may have some degree of lactose intolerance. If there is insufficient lactase, the milk sugar is not digested, resulting in diarrhea, cramps, abdominal gas, and rumbling sounds. In babies or young children who are fed mostly cow's milk, there also may be weight loss or failure to gain. Although lactase deficiency is the most common of the carbohydrate malabsorption syndromes, there also may be a lack of other enzymes needed to absorb different sugars (disaccharides), resulting in symptoms similar to those of lactose intolerance.

Lactose intolerance is suspected when the symptoms invariably occur after consuming milk or milk products. Diagnosis is confirmed by a lactose tolerance test, in which a lactose drink is given and then the patient monitored for gastrointestinal symptoms, such as diarrhea and cramps. There also will not be the usual rise in blood glucose (sugar) that follows consumption of lactose. Other tests may include an analysis of the stools for a high acid content.

Lactose intolerance is treated by avoiding cow's milk and other products that may contain lactose. Babies will be given a formula based on soy or other milk substitutes. There are also milk products in which the lactose is predigested. Also, yogurt and certain cheeses usually can be tolerated because the lactose already has been broken down.

**Celiac Disease.** Celiac disease is a hereditary disorder involving an intolerance to gluten, a protein found in wheat and rye flours. It usually appears in childhood, although there are cases in which it is not diagnosed until adulthood. Symptoms include a



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## Lipomas

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**Last Updated:** August 16, 2002

**Synonyms and related keywords:** liposarcomas, pseudolipoma, teratoma, adenolipomas, angiolipomas, hamartoma, cardiac lipomas

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### INTRODUCTION

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Lipomas are the most common soft tissue tumor. They are slow growing benign tumors of fatty tissue that form a lobulated soft mass enclosed by a thin fibrous capsule. Lipomas may rarely undergo sarcomatous change; however, the event has never been convincingly documented.



**Problem:** Lipomas may easily be confused with other tumors for the following reasons:

Because liposarcomas occur most commonly in the retroperitoneum and on the legs, a tissue diagnosis is indicated in tumors at these locations to exclude the possibility of a malignancy.

A lipoma located in the breast is mammographically radiolucent and can be confused with a pseudolipoma, the soft tissue mass that may surround a small scirrhous cancer.

Conversely, lipomatous lesions in the adrenal gland that have calcifications on radiological examinations have been confused with teratoma.

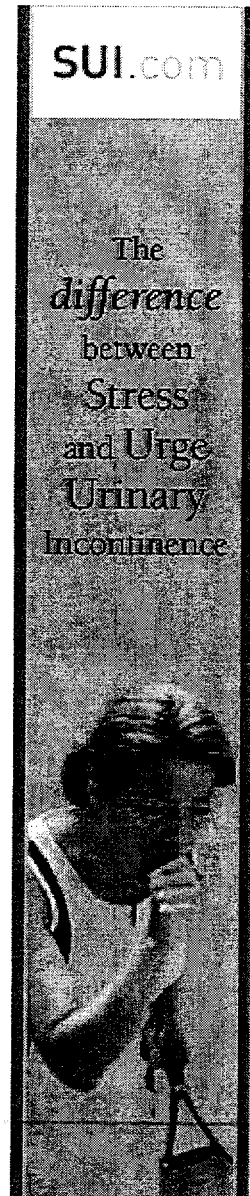
A lipoma of the liver has been confused with a metastasis in a patient with anamnestic adenocarcinoma of the colon.

A palpable inguinal mass without an identifiable hernia defect at time of laparoscopy may indicate the presence of a lipoma of the spermatic cord.

**Frequency:** Lipomas occur in 1% of the population. In the intestine, lipomas constitute 16% of benign small neoplasms, which is less than leiomyomas (18%) and more than adenomas (14%).

**Pathophysiology:** Lipomas may develop in virtually all organs throughout the body. More than half of all gastrointestinal lipomas are in the esophagus, stomach, and small intestine. They are submucosal tumors of adipose tissue, they occur most commonly in the ileum, and they may be single or multiple. Duodenal lipomas are mostly small but may become pedunculated with obstruction of the lumen. They may cause pain, obstructive jaundice, or intussusception in younger patients. Mucosal erosions over the lipoma may lead to severe bleeding. Lipomas in the small intestine occur mainly in elderly patients. They tend to be pedunculated, with some being submucosal, and they are more often found in the ileum than in the duodenum or jejunum. As with duodenal lipomas, severe hemorrhage or intussusception may occur. Colonic lipomas are usually discovered on endoscopy. They may cause pain with obstruction or intussusception.

Lipomas may develop at other rare locations, as reported by numerous case reports. Lipomas have been described in the adrenal gland, the parotid gland, the parapharyngeal space, the mediastinum, the pleura, the major airways, the heart (causing ventricular tachycardia), in the superior vena cava, the spermatic cord, the brain, and at intraspinal locations. Childhood lipomas have been reported at rare locations such as the mesenterium or the esophagus, causing respiratory distress.



Lipoma variants include lipoblastomas and hibernomas. Lipoblastomas occur almost exclusively in infants and children. They have a benign clinical course with a low recurrence rate after surgical excision. Hibernomas, also rare, derive their name from the morphologic resemblance to the brown fat of hibernating animals. They presumably arise from fat that may occur in the back, hips, or neck in adults and infants.

**Clinical:** Lipomas are most often asymptomatic. When they arise from fatty tissue between the skin and deep fascia, typical features include soft fluctuant feel, lobulation, and the free mobility of overlying skin. Symptoms depend on location and can include the following:

- Patients with esophageal lipomas can present with obstruction, dysphagia, regurgitation, vomiting, and reflux; esophageal lipomas can be associated with aspiration and consecutive respiratory infections.
- Lipomas in the major airways can cause respiratory distress related to bronchial obstruction. Patients may present with either endobronchial or parenchymal lesions.
- Lipomas arising from fat in the intramuscular septa cause a diffuse palpable swelling, which is more prominent when the related muscle is contracted.
- Lipomas occur frequently in the breast but not as frequently as expected considering the extent of fat that is present.
- Lipomas in the intestines (ie, duodenum, jejunum, colon) may cause abdominal pain from obstruction or intussusception, or they may become evident through hemorrhage.
- Cardiac lipomas are located mainly subendocardially, rarely intramurally, and are normally unencapsulated. They appear as a yellow mass projecting into the cardiac chamber.
- Lipomas may arise from the subcutaneous tissues of the vulva. They usually become pedunculated and dependent.

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\*• Lipomas are removed for the following reasons:

- Cosmetic reasons

- ✎ ○ To evaluate their histology, particularly when liposarcomas must be ruled out (important in mediastinal tumors)
- ✎ ○ When they cause symptoms
- ✎ ○ When they grow and become larger than 5 cm
- ✎ • Obtain biopsies of large lipomas or those tethered to fascia to rule out a liposarcoma.

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### Relevant Anatomy:

- The anatomy depends on the tumor site.
- Subcutaneous lipomas are usually not fixed to the underlying fascia.

**Contraindications:** No contraindications to removing a lipoma exist, unless the patient is unfit for surgery.

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### Imaging Studies:

- Imaging studies for lipomas include ultrasonography, computerized tomography scans, and magnetic resonance imaging.
- MRI has been recommended as a reliable preoperative investigation.
  - It has been employed in intramuscular lipoma, pediatric lipoblastomas, and others. The findings of intramuscular lipomas, for example, vary from small homogeneous masses to large inhomogeneous lesions with infiltrative margins.
  - However, similar to computed tomography scan, MRI does not allow an absolute reliable distinction between a lipoma and a liposarcoma.
- When computerized tomography scan is employed, Hounsfield units less than 50 are indicative for a soft tissue tumor composed of fat, although no discrimination can be made between a benign lipoma and a malignant liposarcoma.

- Because lipomas are radiolucent, soft tissue radiographs may be indicated when the diagnosis is in doubt.

### Diagnostic Procedures:

- Biopsies are normally not indicated because the entire tumor is usually removed.
- All imaging techniques have been combined with fine-needle aspiration.
- Obtaining tissue samples from different tumor components is important.

### Histologic Findings:

- Lipomas are benign mesenchymal tumors derived from adipocytes. Several variants have been described, including the following:
  - Adenolipomas, a variation of lipomas that may occur in the breast, often have a marked fibrotic component. They are best regarded as hamartoma.
  - Angiolipomas contain many small vessels.
  - Cardiac lipomas may calcify following fat necrosis. Microscopically, they are comprised of fatty tissue with interlacing muscle fibers.
- Fine-needle aspiration biopsies of a lipoblastoma contain multivacuolated lipoblasts, myxoid areas, and a plexiform capillary network.

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### Medical therapy:

- Medical therapy includes endoscopic excision of tumors in the upper gastrointestinal tract (ie, esophagus, stomach, duodenum) or the colon.
- Colonoscopic snare removal has been described but may be associated with perforation if the base is broad.
- Japanese authors reported a safe technique using a bipolar snare and clipping the mucosa of the defective region. Otherwise, surgical extirpation is indicated.

**Surgical therapy:** Radical surgical excision is essential to prevent local recurrence. The therapy depends on the location of the tumor.

- Local removal is indicated in lipomas narrowing the major airways. Lipomas of the lung



are locally excised, which may include resection of parenchyma or the involved airway.

- Local removal is indicated in intestinal lipomas causing obstruction.
- If esophageal lipomas cannot be endoscopically removed, surgical excision is indicated.
- Breast lipomas are excised if their nature is in doubt.
- Intestinal, particularly duodenal, lipomas should be removed either endoscopically or surgically because they can cause obstruction, jaundice, or hemorrhage. A solitary case of a liposarcoma in the ileum has been described.
- Subcutaneous lipomas may be removed by liposuction.
- Lipomas of the vulva are locally excised.

**Preoperative details:** Because all lipomas are radiolucent, findings on soft tissue radiographs can be diagnostic but are only indicated when the diagnosis is in doubt.

**Intraoperative details:**

- Tumors can usually be enucleated. They may recur if not properly removed.
- A man presenting with a frontalis-associated subfascial lipoma as a protruding mass on the lateral forehead may be difficult to dissect because of the highly vascular muscle that invests it.

**Follow-up care:** The patient should consult a physician if signs of recurrence appear.

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Complications caused by lipomas include luminal obstruction or hemorrhage.

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Outcome and prognosis are excellent because lipomas are benign. Recurrence is uncommon at the same location.

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Liposuction may be employed more often in small facial lipomas because favorable aesthetic results have been obtained through strategically placed incisions. Liposuction is indicated for the treatment of medium (ie, 4-10 cm) and large (ie, >10 cm) lipomas; in small lipomas, no advantage has been reported because these tumors can be extracted through small incisions.

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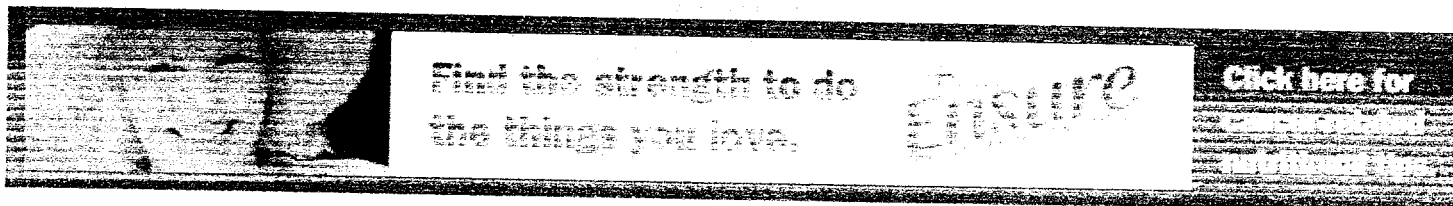
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## Fibroids

By M. Sara Rosenthal, PhD  
WebMD Medical Reference  
from "The Gynecological  
Sourcebook"

**FIBROIDS ARE BENIGN** (noncancerous) tumors that grow inside your uterus. They can be miserable to have, but they usually don't pose any danger to your gynecological health and are quite harmless. It is not the fibroids themselves that are questionable and controversial—instead, it is the method used to treat them. A hysterectomy is still the treatment recommended for most women with fibroids. In fact, fibroid tumors are the most common reason for hysterectomies in North America, accounting for 30 percent of all hysterectomies performed in the country, about 200,000 hysterectomies per year.

Fibroid tumors are one of the most common gynecological complaints. For the majority of women, fibroid symptoms are minor or nonexistent, but 40 percent of women who have fibroids experience such symptoms as an enlargement of the uterus, abnormal uterine bleeding, pelvic pain, and infertility. The size of uterine fibroids can vary from that of a pinhead to larger than a melon. In fact, fibroid weights of more than twenty pounds have been reported.

Most fibroids occur in women of reproductive age; they are diagnosed in African American women two to three times more frequently than in Caucasian women. It is currently believed that obesity has a lot to do with fibroid development. Because fat cells make estrogen, women who are obese are more prone to estrogen-dependent conditions, which include fibroids. It has also been observed that women who have never been pregnant are at higher risk for fibroids than women who have had children; this has to do with the fact that women who have not had children have not had a break from ovulation and, hence, estrogen production.

Although there are some fibroid cases that do warrant a hysterectomy, with current technology most women with fibroids can avoid radical surgery and their reproductive organs can be left intact.

### What Are Fibroids?

The term *fibroid* is actually medical slang. The correct medical term for what we've come to know as a fibroid is *leiomyoma uteri*. The word *fibroid* is really just an adjective that refers to anything fibrouslike or

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resembling a fibroma, a benign tumor made of connective tissue, like muscle. So, describing a tumor as "fibroid" is like describing a sweater as "cotton"—it's simply referring to the fabric of which the tumor is made. This means that a fibroid tumor can exist anywhere in the body, not just in the uterus.

Leiomyoma uteri is a benign tumor made of smooth uterine muscle. *Leio* means "smooth," *my* means "muscle," and *oma* means "benign growth." In general, muscle tumors called leiomyoma can also be found in the stomach and other parts of the body, but the uterus is the most common site. In fact, the uterus consists mainly of muscle. A tumor is essentially a clump of abnormal cells that form a lump, cyst, or mass. It usually starts with one cell that reproduces again and again. Why these cells develop in the first place is still a mystery. When these cells are benign, they are harmless. When these cells go awry, however, they develop into a clump within the myometrium, the smooth muscle coat of the uterus, which forms the main part of the organ. Fibroid tumors are therefore a collection of innocent uterine muscle cells that form a noticeable hard lump.

Fibroids develop most commonly in women who are in their thirties and forties, but they can also develop earlier or later than this. In fact, about 30 percent of all women will develop fibroids by the time they reach thirty-five. An estimated 20 percent of white women and 50 percent of black women over thirty years old have fibroids.

Fibroids are grayish white, firm, round, and ring shaped. They come in all sizes, and it's common to have several fibroids growing at once. The main problem is that once fibroids develop, they may continue to grow, and even if they're surgically removed, there's a 10 percent chance they'll grow back. This is the main reason why so many doctors recommend hysterectomies for women with fibroids.

Fibroids are classified by location:

- *Intramural or interstitial*: fibroids in the outer or innermost layer of the uterus.
- *Subserous/serosal*: fibroids that protrude into the abdominal cavity and can be pedunculated (they grow on a stalk, like broccoli).
- *Submucosal*: fibroids that invade the endometrium.
- *Parasitic*: fibroids that migrate out of the uterus and invade the cervix or other pelvic organs, developing their own blood supply.

### What Causes Fibroids?

Nobody knows why fibroids develop. What we do know is that estrogen can trigger fibroids and may make the fibroids grow more quickly. Just as estrogen triggers the uterine lining, or endometrium, to grow and thicken during the estrogen peak in the menstrual cycle, it also triggers the myometrium to grow and thicken, which is where the fibroids are located. So it's not surprising that the fibroids will grow, too, since they consist of uterine muscle tissue.

After menopause, the fibroids will usually shrink. So if you're only a few years away from menopause and you've just developed fibroids, they may shrink on their own without treatment. If you're taking estrogen synthetically as a hormonal contraceptive, going off the contraceptive will often shrink your fibroids as well. A fibroid may not shrink after menopause (or may first develop after menopause) if you are on hormone replacement therapy (HRT). Some evidence currently suggests that estrogenic chemicals are responsible for an increase in estrogenic conditions such as fibroids, endometriosis, as well as reproductive



cancers. Estrogenic chemicals are man-made chemicals in our environment that break down into by-products that mimic the female hormone estrogen. A good resource on this subject is *Our Stolen Future*, coauthored by Dr. Theo Colborne, a senior scientist with the World Wildlife Fund.

### **Are Fibroids Dangerous?**

Not at all. Basically, a fibroid is to your uterus what a callus is to the heel of your foot. The callus will keep growing and getting thicker until you cut it off. Even after you cut it off, the callus sometimes grows back.

Imagine, though, what would happen if the callus grew so large that it interfered with your balance and walking. If this were the case, you would need treatment so that you could walk properly again. Depending on their location within the myometrium, fibroids can grow so large that they can press against other reproductive organs and interfere with your pelvic functions. You might experience lower abdominal or back pain or even urinary problems. Menstruation can become heavier, with a gushing flow or clots that could predispose you to anemia. Sometimes these heavier periods are accompanied by more painful cramps, but cramps are often not a symptom. In some cases, the cause of the heavier bleeding is not completely understood. Although fibroids may cause abnormal bleeding between periods, this may be a symptom of another problem and should be evaluated before the bleeding is blamed on the fibroid. In other words, if you have fibroids and are bleeding between periods, you should be checked for other causes of abnormal bleeding. An extremely large fibroid may interfere with a pregnancy simply because it takes up too much space. In fact, fibroids have been known to grow so large that they can make a woman appear to be in her twentieth week of pregnancy. But for the most part, fibroids that large are rare. The average large fibroid usually will not interfere with either conception or pregnancy.

Other symptoms of fibroids include a tender or achy feeling in your uterus or laborlike pains (sometimes the fibroid dies when its blood supply is cut off and the uterus tries to expel it). Pressure in the back of your legs or lower abdomen, backaches, painful intercourse, frequent urination, incontinence, and repeated urinary tract infections are other symptoms.

Just as you can have several calluses on your foot, you can also have several fibroids in your uterus. Keep in mind, though, that fibroids generally are of small to medium size and are symptomless. Women with symptomless fibroids can coexist peacefully with them and are not in any danger. Currently, about 40 percent of all reproductive-age women have one or more fibroid tumors, but only about half of these women experience any symptoms.

### **Diagnosing and Treating Fibroids**

If you do notice any of the symptoms described earlier, you have symptomatic fibroids. See your doctor and request a full pelvic exam that includes a rectal exam. Unless a rectal exam is done, your doctor can miss the fibroid. Large fibroids can usually be felt in a pelvic exam. Depending on where they're located, smaller fibroids can also cause symptoms, particularly if you have numerous small fibroids. Generally, an ultrasound test or a laparoscopy will confirm whether or not you have smaller fibroids. If you have abnormal bleeding, then an endometrial biopsy should be done to rule out a hormonal deficiency. Hysteroscopy (in which a telescope is passed through the cervix) can determine whether there are more fibroids on or under the uterine lining. Sometimes these fibroids can be removed through the hysteroscope. Treatment for

symptomatic fibroids is discussed further on.

What if you suspect you have fibroids but have no symptoms? If this is the case, you don't need to do anything until the fibroids start to bother you. If the fibroids grow larger and you develop symptoms later on, then you can see your doctor and confirm whether you have them.

Often, symptomless fibroids are discovered by your doctor accidentally during a routine pelvic exam. If this happens, just ask him or her to keep an eye on the fibroid(s). Then see your doctor every six months instead of annually for a thorough pelvic exam. The bottom line is that if the fibroid isn't bothering you, then you don't need to bother it.

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